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EXAMINER	
RAE, CHARLESWORTH E	
ART UNIT	PAPER NUMBER
1611	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/784,145	MIYACHI ET AL.	
	Examiner	Art Unit	
	CHARLESWORTH RAE	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/26/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments, filed 12/04/07, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

Response to applicant's arguments/remarks

Nonstatutory obviousness-type double patenting (ODP) rejections

Applicant contends that these rejections should be withdrawn for essentially the same summarized reasons (see applicant's Remarks received 12/14/07, pages 1-6):

1) The copending application that forms the basis of each of the OPD rejection made of record in the Office action mailed 6/14/07 at pages 2-7 do not teach or suggest MGUS, SMM, or MM and therefore the instant claimed invention would not be obvious in view of the claimed subject matter of said copending applications.

2) Elan Pharma does not cure the deficiency of the copending applications.

In response, the rejections are maintained as applicant's arguments are not found to be persuasive for the reasons previously made of record in the Office action mailed 6/14/07.

112, 2nd rejection (see applicant's Remarks received 12/14/07 at pgs. 6-7)

Applicant contends that this rejection should be withdrawn in view of the claim amendment.

This rejection is withdrawn

Scope of enablement rejection under 112, 1st para (see applicant's Remarks at pgs. 7-11)

This rejection is withdrawn in view of applicant's amendment.

Written description rejection under 112, 1st para (see applicant's Remarks at pgs. 11-12)

This rejection is withdrawn in view of applicant's persuasive arguments.

Rejection under 102(b) (see applicant's Remarks at pgs. 12-13)

Applicant contends that this rejection should be withdrawn for essentially the following summarized reasons:

1) Elan fails to explicitly or implicitly recite or refer to the adverse event of MGUS, SMM, or MM that may be caused by zonisamide.

2) Elan does not explicitly or implicitly recite or suggest informing a patient or patient's guardian that zonisamide may cause an adverse event of MGUS, SMM, or MM, or informing a patient or patient's guardian of the symptoms associated with the

adverse event of MGUS, SMM, or MM, or informing a patient that prompt medical evaluation is required for the adverse event of MGUS, SMM, or MM.

In response, this rejection is maintained as applicant's argument are not found to be persuasive for the reasons made of record in the Office action mailed 6/14/07 at pages 16-18 and for the following additional reason(s):

1) Zonisamide is well known drug in the art that has been used in the treatment of seizures. The instant claims are also directed to a method of using zonisamide for treating seizures, which overlaps with the cited prior art. Also, the doses of zonisamide encompassed by the instant claims overlap with the doses of zonisamide taught by the cited prior art. To the extent that the therapeutic properties and adverse effects of zonisamide are inseparable from each other, the contemplated treatment effects achieved following the step of administering zonisamide as claimed is the instant claims are deemed to be inherent features of practicing the instant claimed method.

2) The steps of informing the patient or the patient's guardian as claimed in the instant invention are statements of intended use which are not related in such a way to materially affect the functional characteristics of the claimed method of using zonisamide as an adjunctive therapy for treating patients with partial seizures. To the extent that a patient or a patient's guardian may be reasonably informed via various media e.g. verbally, package inserts, electronically, someone of skill in the art would not reasonably or predictably envisage that the instant claimed steps of informing a patient or guardian about zonisamide-induced MGUS, SMM, or MM would have any material or

functional effects in altering the contemplated effects to be achieved in practicing the instant claimed methods. Thus, it is the examiner's position that the steps of simply informing a patient or a patient's guardian about zonisamide-induced MGUS, SMM, or MM, do not confer any patentable weight to the claimed method of using zonisamide as an adjunctive therapy for partial seizures.

Rejection under 103(a) (see applicant's Remarks, pgs. 13-14)

Applicant contends that this rejection should be withdrawn for essentially the following summarized reasons:

1) Elan does not explicitly or implicitly recite or refer to the adverse event of MGUS, SMM, or MM that may be caused by zonisamide. Elan does not provide any teaching or suggestion of any symptoms that would be associated with the adverse event of MGUS, SMM, or MM.

2) To the extent that the PTO may be relying on Asai et al, *Internal Medicine,* 41(2):138-141 (2002) to support the obviousness rejection, the Examiner's reliance on said referene to support a 103(a) rejection and a lack of enablement rejection is contradictory.

3) Kyle does not cure the deficiencies of Elan or Asai as Kyle is a review paper concerning monoclonal gammopathies that discusses methods for analyzing serum proteins and providing a differential diagnosis of monoclonal gammopathies. Kyle does not indicate whether the development and testing of the monoclonal gammopathies has

any relation to naturally occurring monoclonal gammopathies or to drug-induced adverse events of monoclonal gammopathies. More particularly, Kyle does not provide any teaching or evidence that monoclonal gammopathies may be an adverse event/disease associated with zonisamide. The relationship between the adverse event and the drug is critical information (only described and claimed in the present application) that Kyle does not provide.

In response, the rejection is maintained as applicant's arguments are not found to be persuasive for the reasons made of record in the Office action mailed 6/14/07 at pages 18-22 and for the following additional reason(s):

1) Zonisamide is well known in the art as a drug for use in the treatment of seizures. The instant claims are also directed to a method of using zonisamide for treating seizures. Asai et al. disclose a case of a 39-year old man who was suspected of developing hyperlipoproteinemia and smoldering myeloma while being treated with zonisamide; the patient's M-protein did not increase over the 13 months the patient was taken off zinosamide and placed on valproate (abstract) (Asai et al. Smoldering myeloma associated with zonisamide treatment. Internal Medicine. 2002;41(2):138-141). As applicant asserts, the instant invention is directed towards a method of informing a patient or a patient's guardian of zonisamide-induced MGUS, SMM, or MM, which is construed to satisfied by the teaching of Asai et al. To the extent that the therapeutic properties/adverse effects of zonisamide are coextensive with the administering of said drug, coupled with the fact that it is routine in the medical art to

counsel/inform patients about potential side/adverse effects associated with the medications their physicians prescribe, it would have been obvious to someone of skill in the art at the time the instant invention was made combine the teachings of the cited references to create the instant method of informing patients or patient's guardian of any and all potential zonisamide-induced side/adverse effects, including drug-induced monoclonoal gammopathies.

2) The steps of informing the patient or the patient's guardian as claimed in the instant invention are statements of intended use which are not related in such a way to materially affect the functional characteristics of the claimed method of using zonisamide as an adjunctive therapy for treating patients with partial seizures. To the extent that a patient or a patient's guardian may be reasonably informed via various media e.g. verbally, package inserts, electronically, someone of skill in the art would not reasonably or predictably envisage that the instant claimed steps of informing a patient or guardian about zonisamide-induced MGUS, SMM, or MM would have any material or functional effects in altering the contemplated effects to be achieved in practicing the instant claimed methods. Thus, it is the examiner's position that the steps of simply informing a patient or a patient's guardian about zonisamide-induced MGUS, SMM, or MM, do not confer any patentable weight to the claimed method of using zonisamide as an adjunctive therapy for partial seizures.

Nonstatutory Obviousness-Type Double-Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the

unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The above discussion of the ODP rejection in connection with Response to applicant's arguments/remarks is incorporated by reference.

Claims 1-34 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-38 of copending U.S. Patent Application No. 10/752,523, in view of Elan Pharma, FDA Approved Labeling Text, 03/27/200, U.S. Food and Drug Administration, http:/www,fda.gov/cedr/foi/label/2000/20789lbl.pdf, pages 1-24. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are either anticipated by, or would have been obvious in view of the referenced claims.

In particular, claim 1 of copending application '523 is directed to a method of using zonisamide as an adjunctive therapy for partial seizures to improve the safety of such therapy comprising the step of providing a patient with a therapeutically effective amount of zonisamide and informing the patient of the patient's guardian during the course of zonisamide therapy that muscle stiffness, muscle pain, … fever, discolored urine … require prompt medical evaluation if such symptoms are experienced by the patient.

Elan teaches the following: zonisamide as adjunctive therapy in the treatment of partial seizures in adults with epilepsy (page 6); information for patients (page 10 to page 11) and Patient Information Leaflet (pages 22-24), which is reasonably construed to meet the limitation of the instant claim 1 method step of *"informing the patient … during the course of zonisamide therapy that … renal insufficiency, fatigue, anemia …that require prompt medical evaluation if such symptoms are experienced by the patient"* ; 100 mg capsules, which are reasonably construed to meet the *"unit dose form"* limitation recited in instant claim 3, for example (page 21); capsules are supplied

in bottles of 100, which are reasonably construed to meet the *"multiple doses"* limitation recited in instant claim 4, for example; zonisamide doses of 1**00-600 mg/day are effective** (page 20), which overlaps with the dosage range recited in instant claim 2, for example; patients should contact their physician immediately if they develop signs or symptoms such as sudden back pain, abdominal pain, and/or **blood in the urine** (that could indicate a kidney stone) (page 11); patients with **renal or hepatic disease should be treated with caution, and might require slower titration and more frequent monitoring** (page 10, first paragraph; and page 20, last paragraph to page 21, line 2). Elan teaches that **concomitant administration of phenytoin and carbamazepine** increases zonisamide plasma clearance (page 3, 4th paragraph); someone of skill in the art could reasonably construe this limitation to mean the concomitant administration of a therapeutically effective amount of phenytoin or carbamazepine with zonisamide adjunctive therapy. Instant claim 29 recites the term *"therapeutically effective amount of at least one other anti-epileptic drug."* Elan teach a number of zonisamide side effects/adverse effects, which include **fatigue** (pages 14, and 17), mental slowing (page 17), mental slowing (page16), confusion (page 16), dry mouth/thirst (page 16, and page 18), nystagmus (page 16), paresthesia (page 16), dehydration (page 18), hypertension (page 18), hypotension (page 18), tachycardia (page 18), **anemia** (page 18), **SGOT increased** (page 18), SGPT increased (page 18), lactic dehydrogenase (LDH) increased (page 18), and **hematuria** (page 19).

To the extent that the patient population (i.e. partial seizure patients) and the dose of zonisamide (i.e. 25 mg to 600 mg) of the instant invention overlaps with the

reference, the side effects/untoward effects of zonisamide recited in instant claim 1, for example, are coextensive with its administration. Thus, the instant method is deemed to be an obvious variant of the reference claims.

Thus, claims 1-34 are deemed obvious variants of the limitations of the subject matter claimed in copending application '523.

This is a provisional obviousness-type double patenting rejection because the conflicting claims of the copending applications have not in fact been patented.

Claims 1-34 are also rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-41 of copending U.S. Patent Application No. 10/752,522. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are either anticipated by, or would have been obvious in view of the referenced claims.

In particular, claim 1 of copending application '522 is directed to a method of using zonisamide as an adjunctive therapy for partial seizures to improve the safety of such therapy comprising the step of providing a patient with a therapeutically effective amount of zonisamide and informing the patient of the patient's guardian during the course of zonisamide therapy that dehydration, hyperthermia, muscular rigidity, altered mental status ... require prompt medical evaluation if such symptoms are experienced by the patient. To the extent that the patient population (i.e. partial seizure patients) and the dose of zonisamide (i.e. 25 mg to 600 mg) overlap, the side effects/untoward effects of the drug are coextensive with its administration. Thus, the instant method is deemed to be an obvious variant of the reference claims.

Thus, claims 1-34 are deemed obvious variants of the limitations of the subject matter claimed in copending application '522.

This is a provisional obviousness-type double patenting rejection because the conflicting claims of the copending applications have not in fact been patented.

For the same reasons as stated above, claims 1-34 are also provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-15 of copending U.S. Patent Application No. 10/644,935; claims 1-36 of copending U.S. Patent Application No. 10/752,516; claims 1-39 of copending U.S. Patent Application No. 10/753,957; and claims 1-36 of copending U.S. Patent Application No. 10/752,515. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are either anticipated by, or would have been obvious in view of the referenced claims. These are provisional obviousness-type double patenting rejections because the conflicting claims of the copending applications have not in fact been patented.

In reviewing the continuity data, it is noted that applicant has numerous issued patent and pending applications encompassing the same or similar subject matter of the instant application. Applicant should review all subject matter considered the same or similar, and submit the appropriate Terminal Disclaimer(s). For example, application No. 10/753,955, and 10/753,956.

Claim rejections – 35 USC 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-15 are rejected under 35 USC 102(b) as being anticipated by Elan Pharma (Zonisamide Approvable Labeling, Published 03/27/2000).

No patentable weight is being given to the steps of informing a patient or patient's guardian as recited in claims 1, 6, and 11.

Elan teaches the following: zonisamide as **adjunctive therapy** in the treatment of **partial seizures** in adults with epilepsy (page 6). The term "[a] method of using zonisamide as an adjunctive therapy for partial seizures to improve the safety of said adjunctive therapy" as recited in claim 1; the term "[a] method of using zonisamide as an adjunctive therapy for partial seizures to improve the health of a patient receiving said adjunctive therapy" as recited in claim 6; the term "[a] method of using zonisamide as an adjunctive therapy for partial seizures to reduce the risk of monoclonal gammopathy of undetermined significane (MGUS), smoldering multiple myeloma (SMM), or multiple myeloma (MM) in a patient using zonisamide as said adjunctiive therapy" as recited in claim 11; and the term "[a] method of using zonisamide as an adjunctive therapy for partial seizures" as recited in claim 15 are construed to overlap with the teaching of Elan of zonisamide as adjunctive therapy in the treatment of partical seizures in adults with epilepsy. Elan also teach **information for patients** (page 10 to page 11) and **Patient Information Leaflet** (pages 22-24). Claims 1, 6, and 11 recite steps of informing the patient or patient's guardian. The claimed dosage limitations recited in instant claims 2, 5, 7, 10, 12, and 15 (ranging from 25 mg to 600 mg) overlaps with the doses taught by

Elan of zonisamide 100 – 600 mg/day as being effective (page 20). The term "zonisamide is provided in unit dose form" as recited in instant claims 3, 8, and 13 overlaps with the teaching of Elan of 100 mg capsules (page 21). The term "zonisamide is provided in a unit dose form and in multiple doses to provide for a course of therapy" as recited in instant claims 4, 9 and 14 is construed to overlap with the teaching of Elan of capsules supplied in bottles of 100 (page 20). Elan teaches that patients should contact their physician immediately if they develop signs or symptoms such as sudden back pain, abdominal pain, and/or **blood in the urine** (that could indicate a kidney stone) (page 11) and that patients with **renal or hepatic disease should be treated with caution, and might require slower titration and more frequent monitoring** (page 10, first paragraph; and page 20, last paragraph to page 21, line 2). Elan teaches that **concomitant administration of phenytoin and carbamazepine** increases zonisamide plasma clearance (page 3, 4th paragraph), which impliedly is construed to envisage the concomitant administration of a therapeutically effective amount of phenytoin or carbamazepine with zonisamide adjunctive therapy. Elan teaches a number of zonisamide side effects/adverse effects, which include **fatigue** (pages 14, and 17), mental slowing (page 17), mental slowing (page16), confusion (page 16), dry mouth/thirst (page 16, and page 18), nystagmus (page 16), paresthesia (page 16), dehydration (page 18), hypertension (page 18), hypotension (page 18), tachycardia (page 18), **anemia** (page 18), **SGOT increased** (page 18), SGPT increased (page 18), lactic dehydrogenase (LDH) increased (page 18), and **hematuria** (page 19).

Claim 6 recites the term *"improve the health."* This term given its broadest reasonable possible interpretation is construed to mean the administration of an effective amount of zonisamide as taught by Elan.

Claim 11 recites the term *"reduce the risk"* of MGUS, SMM, or MM. This term given its broadest reasonable possible interpretation is construed to encompass any patient with or without MGUS, SMM, or MM who is treated with zonisamide, which is reasonably satisfed by the teaching of Elan of administering zonisamide to adults with partial seizures.

For the above reasons, instant claims 1-15 are rejected as being anticipated by Elan.

Claim rejections – 35 USC 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 16-34 are rejected as being unpatentable over Elan Pharma (Zonisamide Approvable Labeling, Published 03/27/2000), in view of Asai Asai et al. Smoldering myeloma associated with zonisamide treatment. Internal Medicine. 2002;41(2):138-141), in view of Kyle (Kyle. The monoclonal gammopathies. Clin. Chem. 1994; 40/11(B): 2154-2161).

The above discussion of the rejection of 103(a) in connection with the Response to applicant's arguments/remarks and the discussion of Elan in connection with the above rejection analysis under 102(b) are incorporated by reference.

However, Elan does not specifically mention how to advise the physician or an emergency medical worker to monitor a patient who is prescribed zonisamide as said partial seizure for said one or more symptoms "recommending that a laboratory test for paraproteinemia, M-spike protein in the serum, Bence-Jones proteint in urine, or suppression of normal immunoglobulin levels be performed … if the test reveals an abnormal result for that patient … consider removing, reducing, or tapering off zonisamide dosing in the patient while initiating appropriate supportive therapy.

Claim 16 recites the term *"enhancing the safety profile."* This term is reasonably construed to be an inherent feature of the **information for patients** (page 10 to page 11) and **Patient Information Leaflet** (pages 22-24), as taught by Elan.

Claim 17 recites the term *"improving patient outcome."* This term is reasonably construed to be an inherent feature of the **information for patients** (page 10 to page 11) and **Patient Information Leaflet** (pages 22-24), as taught by Elan.

Asai et al. disclose a case of a 39-year old man who was suspected of developing hyperlipoproteinemia and smoldering myeloma while being treated with zonisamide; the patient's M-protein did not increase over the 13 months the patient was taken off zinosamide and placed on valproate (abstract) (Asai et al. Smoldering myeloma associated with zonisamide treatment. Internal Medicine. 2002;41(2):138-141). Asai et al. disclose a single case of a 39-year old man who developed hyperproteinemia (8.6 g/dl) while on zonisamide alone for treatment of generalized seizure; the index patient received zonisamide 200 mg daily for 5 years, followed by 100 mg daily for 10 years (page 138, column 2) . Laboratory examination showed an elevated serum level of immunoglobulin G (IgG, 3,680 mg/dl) with suppressed levels of IgM (38 mg/dl) and IgA (40 mg/dl); Bence-Jones protein in urine was not demonstrated; and serum levels of creatinine, calcium and B2-microglobulin were not elevated. A review of the index patient's medical record revealed gradual increases of serum total protein from 6.5 g/dl (normal range: 6.5-8 g/dl) in 1993 to 8.2 g/dl in 1998 during treatment with zonisamide (page 138, column 2). Asai et al. disclose that the clinical features of malignant B-lymphocyte or plasma cell disorder were absent, including osteolysis, suppression of hemopoiesis, hypercalcemia and renal dysfunction the patient was diagnosed as having smoldering myeloma (page 140, column 1, first full paragraph). Asai et al. report that use of some anticonvulsants such as phenytoin, phenobarbital and primidone have been associated with multiple myeloma (page 140, column 1, second full paragraph). Asai et al. report that zinisamide was discontinued in the patient and replaced with sodium valproate for treatment of seizure; no increase in

the serum level of total protein nor IgG was observed during the 13 month observation period. Asai et al. disclose that a few patients with IgA and/or IgG deficiency have been reported in association with zonisamide (page 140, column 2, first full paragraph, lines 1-4). Asai et al. recommend a periodical examination of serum levels and patterns of gammaglobulin when patients are receiving zonisamide as well as other convulsants.

Kyle teaches that serum proteins should be analyzed by electrophoresis when multiple myeloma (MM), macroglobulinemia, or amyloidosis is suspected; electrophoresis is also indicated in any patient with unexplained weakness or fatigue, anemia, increased erythrocyte sedimentation rate, back pain, osteoporosis or osteolytic lesions or fracture, immunoglobulin deficiency, hypercalcemia, Bence Jones proteinuria, renal insufficiency, or recurrent infections (page 2154, column 2, third full paragraph). Kyle. The monoclonal gammopathies. Clin. Chem. 1994; 40/11(B): 2154-2161). Kyle teaches that the term monoclonal gammopathy of undertermined significance (MGUS) denotes the presence of an M-protein in persons without evidence of myeloma, macroglobulinemia, amyloidosis, or other related diseases (page 2158, column 1, first full paragraph). Kyle teaches that the interval between the recognition of the M-protein and the diagnosis of a serious disease ranged from 2 to 29 years, but no features at diagnosis were useful for distinguishing patients who did not progress from those in whom a malignant change developed (page 2158, column 1, last line to column 2, line 11).

The limitations with respect to "informing a prescribing physician …," "advising the physician …," "recommending that a laboratory test …," as recited in claims 16, 17, and "providing packaging … along with information providing a warning …," as recited in claims 24, 30, and 32, and "monitoring a patient who is receiving administration of zonisamide …," as recited in claim 33, are reasonably construed to within the scope and knowledge of a skilled artisan in the art. Judicial notice is taken that the packaging and

labeling instructing use of a composition is old and well known. The sole difference between the claimed and prior art articles is the printed matter information means indicating the known adverse effects of zonisamide. However, the printed matter e.g. patient information, does not possess a "functional relationship" with the administering of a therapeutically effective amount of zonisamide as adjunctive therapy in patients with partial seizures, and accordingly, is not granted any patentable weight. Thus, the claimed invention was obvious to one of ordinary skill in the art at the time of the instant invention was made.

Based on the teaching of Kyle that serum proteins should be analyzed by electrophoresis when multiple myeloma (MM), macroglobulinemia, or amyloidosis is suspected and that electrophoresis is also indicated in any patient with unexplained weakness or fatigue, anemia, increased erythrocyte sedimentation rate, back pain, osteoporosis or osteolytic lesions or fracture, immunoglobulin deficiency, hypercalcemia, Bence Jones proteinuria, renal insufficiency, or recurrent infections (page 2154, column 2, third full paragraph), someone of skill in the art at the time the instant invention was made would have been motivated to combine the teachings of of the above cited references to create the instant claimed inventive concept of informing a patient or patient's guardian with partial seizures who is treated with zonisamide of the side effects associated with the use of zonisamide.

Thus, someone of skill in the art at the time the instant invention was made would have found it obvious to create the instant invention with reasonable predictability.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charlesworth Rae whose telephone number is 571-272-6029. The examiner can normally be reached between 9 a.m. to 5:30 p.m. Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http:pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 800-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

23 February 2008

/C. R./
Examiner, Art Unit 1611

/Raymond J Henley III/
Primary Examiner, Art Unit 1614